

Reproducibility of GFR measured by chromium-51-EDTA and iohexol

Pierre Delanaye¹, Etienne Cavalier², Marc Froissart³, Jean Marie Krzesinski¹

¹Department of Nephrology, University of Liège, CHU Sart Tilman, Liège, Belgium

²Department of Clinical Chemistry, University of Liège, CHU Sart Tilman, Liège, Belgium

³Department of Physiology, University of Paris 5 René Descartes, HEGP AP-HP, Paris, France.

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We read with interest the article published by Bird *et al* about the reproducibility of measured GFR by iohexol and Cr-51-EDTA [1]. We would like to make one comment and to share our own results on this fundamental (although understudied) topic. As we already pointed out in a NDT editorial, we share the same reserves about the opportunity to index glomerular filtration rate (GFR) with body surface area [2]. Indexing GFR with extracellular fluid volume (ECV) may be viewed as more logical as one of the major functions of the kidney is to regulate ECV. However, the fact that reproducibility of the GFR is better when indexed with ECV than when indexed with BSA is not the definite proof to use ECV indexation. The only proof would be to have an absolute correlation between GFR and ECV and that this relationship would totally disappear between indexed GFR and ECV [2]. For these reasons, we think that reproducibility of GFR measurement must be calculated from absolute, non-indexed GFR. Can Bird *et al* give the reproducibility of their non-indexed GFR?

We have recently published our data regarding the reproducibility of serum creatinine and cystatin C with concomitant measurement of GFR [3]. Briefly, we have simultaneously measured GFR using the plasma clearance of iohexol and Cr-51-EDTA after 120 and 240 minutes as described by Brochner-Mortensen within a one week interval [4]. Our results in twelve healthy and fasting subjects show a slightly better reproducibility for iohexol (4.5%) than for Cr-51-EDTA (7.4%). Comparing to the Bird *et al* results, our data show relatively the same reproducibility for GFR measured with Cr-51-EDTA (and are somewhat similar to results published previously with 51Cr-EDTA plasma clearances ($9.0 \pm 5.3\%$)[5]), although the reproducibility of GFR measured with iohexol is better. Discrepancies between the results can be explained in part by differences in the methodology of the studies. What is of interest is that we have measured iohexol with a HPLC method. This method is probably more precise than the method used by Bird *et al*, namely X-ray fluorescence. From an analytical point of view, the HPLC method has been strongly and deeply validated (E. Cavalier, submitted), including in the low values (40 to 600 µg/ml), which are routinely measured. In this range, the method used by Bird *et al* seems less precise [6] and, in any case, has not been validated in their figure 1 (notably, the intercept in this figure is far from negligible). "Analytically" speaking, iohexol concentrations lower than 600 µg/ml are not precise enough to be used in the study by Bird *et al*. From our experience, such a level of concentration can be reached with the methodology used in this study (injection of 20 mL Omnipaque® 300). As analytical variance is included in the global reproducibility, this point must be underlined and can explain the better reproducibility observed using the "HPLC" iohexol in our data.

We have no conflict of interest to declare

References

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¹Nicholas J Bird and ²Adrien Michael Peters

¹Addenbrooke's Hospital, Cambridge, and ²University of Cambridge

Sir,

We are grateful to Delanaye et al for their interesting comments concerning indexed GFR.

We would like to make several points.

1. We do not think we claimed that better reproducibility was proof that indexing to extracellular fluid volume (ECV) was better than indexing to body surface area (BSA).
2. We presume that the only available proof referred to by Delanaye et al, namely an absolute correlation between GFR and ECV and its disappearance when using indexed values, refers to indexing with ECV. Correlating GFR indexed to ECV (GFR/ECV) and ECV itself is only valid with an independent measure of ECV, so in our dual indicator studies we examined these relations in 20 normal subjects studied under fasting and non-fasting conditions using GFR measured with one indicator and ECV simultaneously and independently measured *with the other* (1). As would be expected from the variation in subject size, absolute GFR and ECV correlated positively with each other, although only modestly ($n = 40$; $r = 0.66$ and 0.46 when GFR was measured with Cr-51-EDTA and iohexol, respectively). These coefficients are similar to those obtained when GFR was correlated with BSA ($r = 0.57$ and 0.59 , respectively), although allowance should be considered for the fact that measurement of BSA is probably more precise than that of ECV. GFR/ECV, however, correlated inversely with ECV/BSA (but inconsistently; thus only when the former was measured with iohexol and the latter with Cr-51-EDTA but not *vice versa*), whereas GFR/BSA correlated positively with ECV/BSA (but only when the former was measured with Cr-51-EDTA and the latter with iohexol) (1). We interpreted this to be consistent with the notion that, in normal subjects, expansion of ECV leads to a corresponding increase in GFR/BSA but that this increase is not proportionate, leading to a fall in GFR/ECV.
3. In any event, reproducibility of non-indexed fasting GFR will be the same as indexed GFR unless BSA changed between the 2 studies. Since these were close together, it did not.

We would agree that, in general, the poorer reproducibility we found with iohexol was probably the result of the X-ray fluorescence (XRF) method we used. We did implement an HPLC method, in parallel with XRF, towards the end of our study and recorded reproducibility data for 3 subjects that were extremely promising.

Yours

1. Bird NJ, Peters C, Michell AR, Peters AM. Association between glomerular filtration rate and extracellular fluid volume in normal subjects and patients with renal impairment. *Scand J Clin Lab Invest* 2008; 68: 39-49.